

Oral muscles are progressively affected in Duchenne muscular dystrophy: implications for dysphagia treatment

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Abstract Dysphagia is reported in advanced stages of Duchenne muscular dystrophy (DMD). The population of DMD is changing due to an increasing survival. We aimed to describe the dysphagia in consecutive stages and to assess the underlying mechanisms of dysphagia in DMD, in order to develop mechanism based recommendations for safe swallowing. In this cross-sectional study, participants were divided into: early and late ambulatory stage (AS, $n = 6$), early non-ambulatory stage (ENAS, $n = 7$), and late non-ambulatory stage (LNAS, $n = 11$). Quantitative oral muscle ultrasound was performed to quantify echo intensity. Swallowing was assessed with a video fluoroscopic swallow study, surface electromyography (sEMG) of the submental muscle group and tongue pressure. Differences in outcome parameters among the three DMD

stages were tested with analysis of variance. Oral muscles related to swallowing were progressively affected, starting in the AS with the geniohyoid muscle. Tongue (pseudo) hypertrophy was found in 70 % of patients in the ENAS and LNAS. Oral phase problems and post-swallow residue were observed, mostly in the LNAS with solid food. sEMG and tongue pressure data of swallowing solid food revealed the lowest sEMG amplitude, the longest duration and lowest tongue pressure in the LNAS. In case of swallowing problems in DMD, based on the disturbed mechanisms of swallowing, it is suggested to (1) adjust meals in terms of less solid food, and (2) drink water after meals to clear the oropharyngeal area.

Keywords Duchenne muscular dystrophy · Dysphagia · Oral muscles · Ultrasound · Video fluoroscopic swallow study · Surface electromyography

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Introduction

Duchenne muscular dystrophy (DMD) is the most frequent neuromuscular disorder occurring in childhood, characterized by a progressive loss of muscle cells and replacement by interstitial fat and fibrosis in the affected muscles [1]. This is due to mutations of the dystrophin gene (locus Xp21.2) resulting in an absence of the protein dystrophin. DMD is clinically characterized by progressive muscle weakness and loss of ambulation between the age of 9 and 13 years, loss of the arm function between the age of 13 and 16 years, and eventually life-threatening cardiac and pulmonary complications if untreated [2].

Feeding, chewing and swallowing difficulties have been reported in the advanced stages of DMD [3–6]. Video fluoroscopic swallow studies (VFSS) demonstrated effortful

bolus transport for solid food with pharyngeal residue when the age of DMD patients increases. The pharyngeal phase of swallowing seemed well triggered by the central nervous system, but the range of hyoid movement was reduced, indicative of some progressive muscle weakness associated with swallowing [5]. As DMD patients survive longer, swallowing problems will become a more prominent feature.

A VFSS is the gold standard for evaluation of dysphagia, but it is insufficient to identify biomechanical events in the oral and pharyngeal phases of swallowing [7]. Other techniques, such as measuring tongue pressure and surface electromyography (sEMG) of the submental muscle group during swallowing, can be applied as quantitative measurement methods to collect clinically relevant information on swallowing [8–10].

Previous studies have shown that structural muscle changes caused by neuromuscular diseases can be detected by muscle ultrasound and quantitative muscle ultrasound (QMUS) can be used to quantify the changes in muscle architecture [11]. Normal striated muscle tissue is hypo-echogenic and is depicted as relatively black. Diseased muscles gradually become whiter due to increased echo intensity, because normal muscle tissue is replaced by fat and fibrosis [12]. Ultrasound is a quick and non-invasive method, and can easily be used in children. QMUS of tongue and submental muscles proved to be feasible in healthy children and young adults, which could serve to detect differences with DMD patients [13]. Based on the findings of Aloysius et al. [5] this study focuses on the underlying mechanisms of dysphagia in the oral phase, and of the post-swallow residue in the pharyngeal phase.

In order to develop mechanism based recommendations [14] for efficient and safe feeding and swallowing, we designed a cross-sectional study to (a) describe the dysphagia in consecutive stages in boys and adults with DMD, and (b) determine the underlying mechanisms of dysphagia in DMD. To this end, the oral muscle structures and different aspects of swallowing were assessed.

Methods

Patients

The study was conducted at the Radboud University Medical Centre in Nijmegen, The Netherlands, between July 2010 and June 2011. Patients with DMD were recruited from the pediatric centre for neuromuscular diseases, and by announcements of patient organizations. Patients with and without swallowing problems were invited to participate. Only patients with an established diagnosis of DMD older than 5 years were eligible. Patients were excluded if

they were totally dependent on tube feeding. The Motor Function Measure scale was performed to evaluate the sitting position, arm function, and neck and head control [15]. This information was used to divide the participants in three groups based on the major clinical stages of DMD [2]: AS; ENAS (able to maintain posture); LNAS (upper limb function and postural maintenance is increasingly limited).

This study was approved by the Committee on Research Involving Human Subjects of Arnhem and Nijmegen for the experiments using human subjects and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Eligible patients or, if they were <12 years their parents, were sent an information letter with an invitation to participate in the study. After receiving their informed consent, they were invited to come to the hospital for 1 day.

Procedures

Information was collected on the use of medications (i.e., prednisone and antibiotic therapy for pneumonia, proven with a chest X-ray, in the past year), ventilation support and scoliosis surgery. Patients were interviewed with a semi-structured questionnaire including complaints about feeding problems [16]. QMUS was performed to measure echo intensity of the anterior belly of the digastric muscle (left and right), the geniohyoid muscles (left and right together), and the longitudinal superior and transverse tongue muscles. A region of interest was selected that included as much muscle tissue as possible, but avoiding the surrounding fascia. Of this region, the mean echo intensity (i.e., mean grey value) was measured using histogram based gray-scale analysis [13]. Additional measurements were done to measure thickness of the digastric muscles and thickness of the tongue. The thickness of the tongue, including the geniohyoid and genioglossus muscles, was measured from the raphe of the mylohyoid muscle to the upper boundary of the tongue. The protocol and the derivation of normal values have been described in an earlier study (Fig. 1) [13]. The data of the DMD patients were compared with these normal values and described as z scores (i.e., the amount of standard deviations below or above the mean of normal values).

Swallowing was assessed with (1) a VFSS, (2) sEMG of the submental muscle group, and (3) anterior tongue pressure (ATP). The tasks consisted of saliva swallowing and three test substances: 5 ml water, 5 ml custard (referred to as thick liquid), and 5 g pureed potato (referred to as solid). Patients were first asked to swallow their saliva twice, taking sufficient time between the swallow acts to replenish the saliva. For each measurement (VFSS, sEMG and ATP separately) the test substances were offered twice and the mean outcome values of the two performances was used.

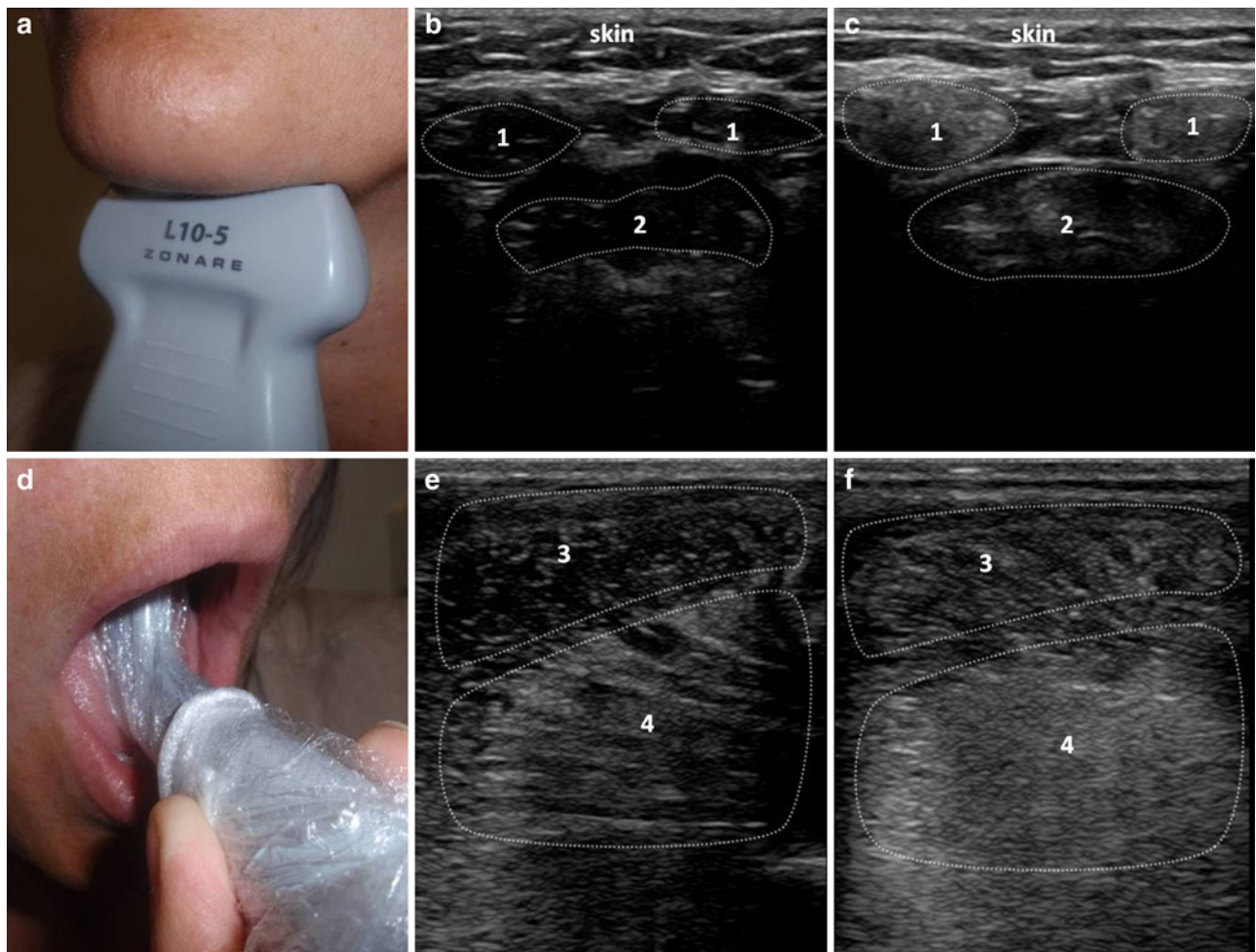


Fig. 1 Transducer placement and related oral muscle ultrasound images. **a** Transducer placement for submental muscles in transverse position with an L10–L5 linear array, gain 78 dB, 8.5 MHz, depth 4 cm (related images **b** and **c**). 1 digastric muscles, 2 geniohyoid muscles. **b** Ultrasound image from a 12-year-old boy with DMD (early non-ambulatory stage, ENAS), digastric muscle left, z score 0.69; digastric muscle right, z score 0.56, geniohyoid muscle, z score 2.56. **c** Ultrasound image from an 18-year-old boy with DMD (late non-ambulatory stage, LNAS) digastric muscle left, z score 6.46; digastric muscle right, z score 5.62, geniohyoid muscle, z score 3.96.

For the VFSS, water was mixed with a water-soluble contrast medium (Xenetix 300 mg, Guerbet, Belgium) and thick liquid and solid were mixed with barium powder (EZHD Barium Sulfate 98 %, Guerbet, Belgium). Continuous fluoroscopy with a pulse rate of 30 pulses/s was used. The video files were captured and stored on the Digital Swallowing Workstation (DSW, KayPentax, Lincoln Park, New York), which allowed for slow-motion and frame-by-frame analysis. A list of 12 findings (Fig. 2) in the oral, pharyngeal and upper esophageal phase, related to underlying physiologic bases of dysphagia, was scored as ‘absent’ or ‘present’ [17]. If residue after swallowing was present, it was observed whether this residue was cleared

d Transducer placement for tongue muscles with an L14–L5sp array, gain 80 dB, 12 MHz, depth 3 cm (related images **e** and **f**). 3 superior longitudinal tongue muscle, 4 transverse tongue muscle. **e** Ultrasound image from a 12-year-old boy with DMD (ENAS), superior longitudinal tongue muscle, z score 0.42, transverse tongue muscle, z score 0.59. **f** Ultrasound image from an 18-year-old boy with DMD (LNAS), superior longitudinal tongue muscle, z score 1.32, transverse tongue muscle, z score 3.38. Note that the images of the 12-year-old boy are almost normal, except for the geniohyoid muscle

with the next dry swallow. If not, patients were asked to take a comfortable amount of water, and it was noted whether this post-swallow residue was cleared. The VFSS registrations were analyzed by the first author and another experienced speech language therapist, who was blinded to the functional status of the patients, at different times. The data for the 12 findings were compared to determine the interrater reliability, which was good (kappa statistics varying 0.71–1.0).

While swallowing saliva, water, thick liquid and solid food, sEMG measurements of the submental muscles and ATP measurements were performed. The standard protocol, previous described by our group, was used [18]. The

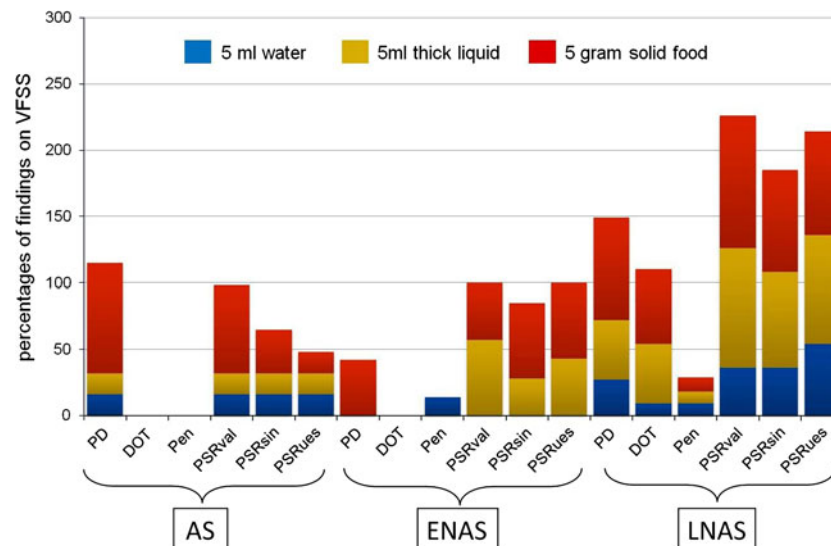


Fig. 2 Percentages of scores on VFSS by DMD stage. The percentages of the findings are the total of the scores observed during swallowing water, thick liquid and solid food together (maximum 300 %). Note that the items from the list of findings [17] ‘loss of food out of the mouth’, ‘material in valleculae preinitiation of swallowing’, ‘pharyngonasal backflow’, ‘aspiration before swallowing’, ‘aspiration during swallowing’, and ‘aspiration after swallowing’ were not

observed. VFSS, video fluoroscopic swallow study; PD, piecemeal deglutition; DOT, delayed oral transport >3 s; Pen, penetration of food above the vocal folds; PSRval, post swallow residue in the valleculae; PSRsln, post swallow residue in the piriform sinuses; PSRues, post swallow residue above or in the upper esophageal sphincter; AS, early and late ambulatory stage; ENAS, early non-ambulatory stage; LNAS, late non-ambulatory stage

sEMG signals were obtained from a single three-point disposable electrode disk (2.25 inch diameter) placed on the suprahyoid region. The electric activity of the submental muscle group during swallowing the test substances was inferred from the mean amplitude value (MAV) of sEMG activity. The signals were processed by the Swallowing Signals Lab of the DSW at a sampling rate of 250 Hz and with an upper recording limit set at 200 μ V. The raw signal was band-pass filtered, integrated, and rectified. Duration (in seconds) and MAV (in μ V) were calculated by the software of the DSW.

ATP data were collected during the swallowing of the test substances. Because the tongue exerts the most force at the front of the palate during swallowing, a two-bulb array was hand-held and placed in the mouth at the alveolar ridge, so that the bulbs were in contact with the tongue. The force, exerted by the tongue on the front of the palate, was measured during swallowing. The pressure signals were processed at a 250 Hz sampling frequency and an upper recording limit of 500 mmHg. Because sEMG and ATP data during swallowing show considerable inter-subject variation, relative changes in sEMG and ATP values were calculated with water as reference value [18, 19].

Statistical analysis

Descriptive statistics were used for patient characteristics, complaints concerning feeding, and findings of the VFSS.

The Pearson correlation coefficient was used to assess the correlation between thickness and echo intensity of the tongue muscles.

One-way analysis of variance was performed to analyze differences between the three DMD stage groups, in each of the following variables, separately: the mean z scores of thickness of the digastric muscles and tongue, and of the echo intensity of the oral muscles. The independent variable was the DMD stage (AS, ENAS, LNAS). Tukey’s contrast test was used to test the differences between the three DMD stages for statistical significance. The estimated mean z score in each DMD stage [with the 95 % confidence interval (CI)] is presented. A linear mixed model for repeated data was used to study the influence of the test substance consistency and of the DMD stages on each of the biomechanical parameters of swallowing, separately. The dependent variable was the logarithmic transformed biomechanical parameter of swallowing: i.e., the MAV, the sEMG duration, and the maximum ATP, respectively. The independent class variables were bolus consistency (saliva, water, thick liquid, solid) and DMD stage (AS, ENAS, LNAS). The independent random variable was the intercept of each patient. This allows different levels for different individuals. The interaction term between bolus consistency and DMD stage was also included in the linear part of the model. The estimated mean values of the swallow parameters for each substance consistency, expressed as a percentage of the water value (with 95 %

CI), were calculated by using the anti-logarithmic transformation.

Results

Twenty-four DMD patients, aged from 6.3 to 41.6 years (median 17.3 years), participated in the study. The patient characteristics are presented in Table 1. Complaints about feeding and swallowing were reported in all stages, but more in the LNAS than in the AS and ENAS.

The echo intensity of the digastric and geniohyoid muscles and the tongue muscles showed a gradual increase, starting in the AS with the geniohyoid muscle (Table 2) (see Fig. 1 for examples). A significant difference among

the three DMD stages was found for the geniohyoid and tongue muscles. The thickness of the digastric muscles showed values within the normal range. In the AS all patients had a tongue thickness within the normal range (z score <2). In the ENAS and LNAS the tongue thickness was abnormal (z score >2) in 70 % of the patients. There was a significant correlation between echo intensity of the superior longitudinal tongue muscle and tongue thickness ($p = 0.001$), and not between the echo intensity of the transverse tongue muscle and tongue thickness ($p = 0.78$).

The findings of the VFSS are provided in Fig. 2. In the oral phase, piecemeal deglutition (i.e., the need for multiple swallows to clear the oral cavity) was observed, mostly with solid food and more in the AS and LNAS than in the ENAS. Only participants in the LNAS showed delayed oral

Table 1 Patient characteristics by DMD stage

	DMD stage		
	AS ($n = 6$)	ENAS ($n = 7$)	LNAS ($n = 11$)
Age (years)	8.3 (6.3–10.5)	13.1 (10.7–20.5)	21.8 (16.2–41.6)
BMI	16 (14–20)	22 (16–29)	21 (15–35)
MFM score ^a	100 (93–100)	93 (30–100)	21 (0–75)
Item 13, maintain sitting position ^b	3 (3)	3 (1–3)	3 (0–3)
Item 14, raise the head from a fully flexed position ^b	3 (3)	3 (1–3)	3 (0–3)
Questionnaire			
Choking thin liquid ^c	1 (0–2)	0 (0–1)	0 (0–3)
Choking solid food ^c	1 (0–1)	0 (0–1)	1 (0–2)
Sticking food in the throat ^c	1 (0–1)	0 (0–1)	1 (0–2)
Chewing problems ^c	0.5 (0–2)	1 (0–2)	2 (1–3)
Duration meal time ^d	0.5 (0–1)	0 (0–1)	2 (0–4)
Self feeding capability ^e	2 (2)	1 (0–2)	0 (0–2)
Medication, Prednisone	5 (83)	4 (57)	1 (9)
Pneumonia ^f	0 (0)	1 (14)	6 (54)
Partial enteral feeding	0 (0)	0 (0)	2 (18)
Ventilatory support	0 (0)	1 (14)	5 (45)
Part-time (nocturnal)	0 (0)	0 (0)	3 (27)
Continuous noninvasive	0 (0)	0 (0)	2 (18)
Continuous with tracheostomy			
Scoliosis surgery	0 (0)	0 (0)	11 (100)

Data are median (range) or n (%). MFM scoring per item: 0, does not initiate movement or starting position cannot be maintained; 1, partially completes the exercise; 2, completes the exercise with compensations, slowness, or obvious clumsiness; 3, completes the exercise with a standard pattern [15]

MFM motor function measure, AS early and late ambulatory stage, ENAS early non-ambulatory stage, LNAS late non-ambulatory stage, BMI body mass index

^a MFM score = percentage of maximum score of the items 13–23 (total score 33 points = 100 %)

^b Separate score on item 13 and 14 of the MFM

^c Items of semi-structured questionnaire [16]. Problems with choking on thin liquid and solid food, the feeling of food sticking in the throat, and chewing problems were scored with a four-point scale: 0, no problems; 1, once a week; 2, once every day; 3, several times a day

^d Problems with duration of meals were scored on a five-point scale: 0, normal; 1, sometimes >30 min; 2, always >30 min; 3, >45 min; 4, >60 min

^e Self-feeding capability: 0, totally dependent; 1, partially self; 2, totally independent

^f Pneumonia, proven with a chest X-ray, in the past year requiring antibiotic therapy

Table 2 The estimated mean z score [95 % confidence interval (CI)] of echo intensity and muscle thickness of the total group and by DMD stage

	DMD stage			
	Total ($n = 24$) mean (95 % CI)	AS ($n = 6$) mean (95 % CI)	ENAS ($n = 7$) mean (95 % CI)	LNAS ($n = 11$) mean (95 % CI)
Echo intensity				
m. digastricus left	2.1 (0.7–3.4)	0.3 (–1.1–1.7) ^b	1.2 (–1.3–3.7) ^b	3.6 (1.3–5.9) ^b
m. digastricus right	2.1 (0.7–3.4)	1.3 (–1.2–1.8) ^b	1.4 (–0.7–3.5) ^b	3.3 (0.7–5.8) ^b
m. geniohyoid	6.3 (4.0–8.5)	2.4 (–0.8–5.5) ^b	5.6 (0.8–10.3) ^{b,c}	8.8 (5.3–12.3) ^c
m. sup. long. ^a	1.9 (0.8–3.0)	–0.3 (–0.8–0.8) ^b	0.7 (–0.2–1.5) ^b	3.7 (1.8–5.6) ^c
m. transversus ^a	0.7 (0.0–1.3)	–0.1 (–1.9–1.7) ^{b,c}	–0.2 (–1.2–0.8) ^b	1.6 (0.7–2.5) ^c
Muscle thickness				
m. digastricus left	1.4 (0.7–2.2)	1.3 (–0.4–2.7) ^b	2.5 (1.4–3.5) ^b	0.9 (0.7–2.4) ^b
m. digastricus right	0.7 (0.1–1.3)	0.7 (–0.6–2.1) ^b	1.4 (0.5–2.3) ^b	0.3 (–0.9–1.4) ^b
Tongue	3.0 (1.9–4.2)	1.1 (0.6–1.5) ^b	2.8 (1.0–4.6) ^b	4.2 (2.0–6.5) ^b

Data are z scores

DMD Duchenne muscular dystrophy, *AS* early and late ambulatory stage, *ENAS* early non-ambulatory stage, *LNAS* late non-ambulatory stage, *m. sup. long.* superior longitudinal tongue muscle

^a Tongue muscles

^{b, c} Differences between the DMD stages were tested with pair wise comparisons. Same characters indicate non-statistically-significant differences between AS and ENAS, between AS and LNAS, or between ENAS and LNAS, according to the Tukey's contrast test

transport. Post-swallow residue was seen more frequently with thick liquid and solid food. With a next dry swallow, thick liquid residue was not cleared in 41 % and solid food residue was not cleared in 45 %. After this dry swallow, one sip of water was enough to clear the remaining residue of thick liquid. The remaining residue of solid food was cleared in 70 % with one sip of water. Two sips of water were needed in 21 %, and one patient (LNAS) needed more sips of water to clear the solid food post swallow residue.

Table 3 shows the estimated mean values with the 95 % CI of the submental muscles activity and ATP during swallowing of the test consistencies by DMD stage. The patterns of the estimated mean percentage change compared to water (95 % CI) of swallowing saliva, thick liquid, and solid food were in large consistent between the AS and ENAS group (Fig. 3). The estimated mean values of the sEMG activity and ATP for the swallowing of saliva showed largely the same pattern as in healthy subjects, with higher MAV, shorter duration and lower ATP, relative to water. The higher ATP for swallowing saliva in the AS group (128, 95 % CI: 96–170) was also found in the healthy participants from 5 to 15 years (129, 95 % CI: 114–146) [18].

No significant differences were found for the estimated mean percentage change compared to water among the DMD stages for the swallowing of thick liquid in the MAV, duration and ATP, respectively. The estimated mean percentage change of MAV compared to water for swallowing solid food was significantly higher in ENAS than

LNAS ($p = 0.05$) and significantly higher in AS than LNAS ($p < 0.001$). The estimated mean percentage change of duration compared to water for swallowing solid food was significantly lower in AS than LNAS ($p < 0.001$) and significantly lower in ENAS than LNAS ($p < 0.001$). Although there is a difference between AS and LNAS for the estimated mean percentage change of ATP compared to water for swallowing of solid food, it did not reach statistically significant difference ($p = 0.5$). For all variables, the LNAS group showed other patterns of percentage change between water, thick liquid and solid food.

Discussion

As survival increases in DMD, a better understanding of the nature and clinical course of dysphagia in this patient group is essential for optimal recommendations and management of feeding. In our cohort of boys and adults with DMD, we found oral phase problems during swallowing and pharyngeal post-swallow residue, more with solid food than with water or thick liquid, which increases with more advanced stages of the disease. These findings are in concordance with the complaints reported by our patients. In this relative small group of 24 patients with DMD, only two patients showed penetration above the vocal folds, but no direct aspiration was observed, indicating normal triggering of the pharyngeal swallow. It was postulated that pharyngeal post-swallow residue was indicative for some progressive muscle weakness [5]. To our knowledge this is

Table 3 The estimated mean value [95 % confidence interval (CI)] of swallowing water and the estimated mean values (95 % CI) of swallowing saliva, thick liquid, and solid food respectively, expressed as a percentage of the water value (%), by DMD stage

	Water	Saliva mean (%) (95 % CI)	Thick liquid mean (%) (95 %CI)	Solid mean (%) (95 %CI)
MAV mean (μV) (95 % CI)				
AS (n = 6)	28 (22–34)	95 (79–115)	109 (90–131)	140 (116–169)
ENAS (n = 7)	21 (17–26)	102 (86–121)	100 (84–119)	138 (116–164)
LNAS (n = 11)	23 (19–26)	97 (84–111)	99 (86–114)	106 (92–122)
Duration mean (s) (95 % CI)				
AS (n = 6)	2.5 (1.8–3.3)	101 (72–141)	128 (91–180)	183 (130–257)
ENAS (n = 7)	2.5 (1.9–3.3)	76 (56–105)	125 (91–171)	192 (140–263)
LNAS (n = 11)	3.4 (2.7–4.2)	90 (70–115)	109 (85–140)	294 (229–379)
ATP mean (mmHG) (95 % CI)				
AS (n = 6)	82 (58–114)	128 (96–170)	124 (95–162)	176 (133–234)
ENAS (n = 7)	134 (99–184)	96 (75–123)	131 (102–168)	123 (96–157)
LNAS (n = 11)	113 (88–145)	95 (78–116)	109 (89–132)	103 (82–128)

The estimates are calculated using a linear mixed model, for each of the following variables: MAV and duration of sEMG activity of the submental muscles, and ATP

MAV mean amplitude value, AS early and late ambulatory stage, ENAS early non-ambulatory stage, LNAS late non-ambulatory stage, ATP anterior tongue pressure

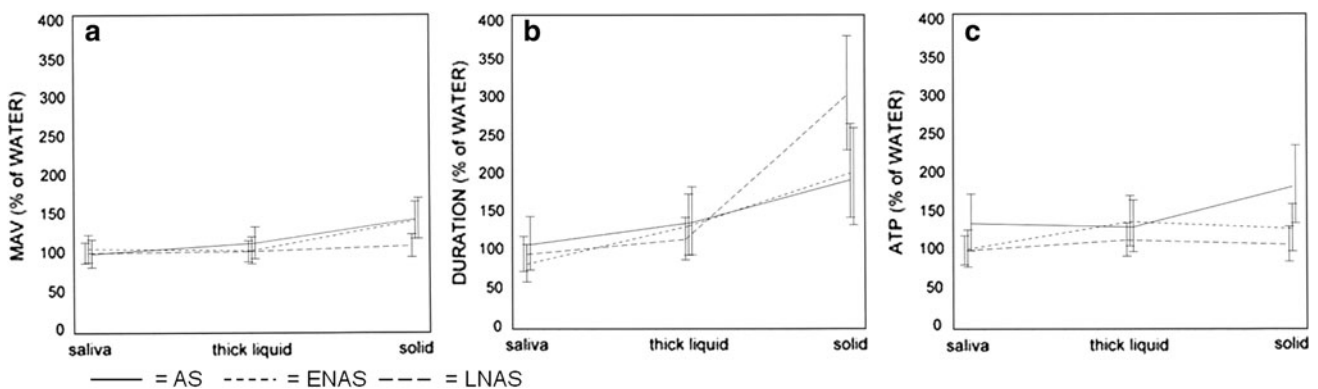


Fig. 3 The estimated mean percentage change, compared to water, of saliva, thick liquid, and solid food. The estimated mean percentage change with the 95 % confidence interval (CI), compared to water, of saliva, thick liquid, and solid food in the MAV (a) and duration (b) of

sEMG activity, and in ATP (c) respectively, by DMD stage. MAV mean amplitude value, ATP anterior tongue pressure, AS early and late ambulatory stage, ENAS early non-ambulatory stage, LNAS late non-ambulatory stage, DMD Duchenne muscular dystrophy

the first study that shows dystrophic changes in oral muscles, related to swallowing, of DMD patients.

During swallowing, tongue pressure applied to the front of the palate and propulsion of the tongue to transport the bolus are essential components. More tongue pressure is needed to swallow solid food compared to swallowing water [18]. On the VFSS, piecemeal deglutition with solid food was observed in all stages, but mostly in the LNAS. Previous research hypothesized that problems with oral transport are related to reduced muscle strength of the tongue [3, 5]. Our ATP data shows the reduced ability of DMD patients in the LNAS to create this higher pressure while swallowing solid food, resulting in disturbed oral transport with a longer duration. This tongue-to-palate

contact is achieved by activation of the tongue muscles in combination with activity of the submental muscles (i.e., the anterior belly of the digastric muscles, geniohyoid and mylohyoid muscles) [20]. Increased echo intensity in limb muscles of DMD boys was related to reduced muscle strength and reduced functional abilities [21]. The increased echo intensity (z scores >2) in the LNAS of the digastric muscles, the geniohyoid muscles and the superior longitudinal tongue muscle reflects the degeneration of these oral muscles [12] and explains their reduced strength, causing the need for multiple swallows to clear the oral cavity when swallowing solid food.

Pharyngeal post-swallow residue was an important finding from the VFSS, starting in the AS and increasing in

the ENAS and LNAS. The submental muscles are pulling the hyoid in an anterosuperior position with protection of the airway and pulling open the upper esophageal sphincter [22]. Aloysius reported a reduced range of hyoid movement in patients with DMD older than 16 years [5], which is strongly associated with an increased risk of post-swallow residue [23]. Compared with swallowing water, a mean increase of 27 % in the MAV of the submental muscles is expected for swallowing solid food [18]. In the LNAS only an increase of 6 % was found, indicating insufficient activity of the submental muscles. We think that the increased echo intensity of the digastric and geniohyoid muscles in the LNAS reflects this reduced submental strength, contributing to a post-swallow residue of solid food. Because this residue is likely to spill into the open airway, it places patients at risk for pneumonia [24]. In 54 % of the patients in the LNAS, medications for pneumonia had been given in the last year, which emphasizes the importance of adjusting meals in this stage of the disease by avoiding solid food and clearing the pharyngeal area with water in case of choking or aspiration pneumonia.

In this study we have shown that oral muscles of the submental area and tongue are not spared in DMD. In the study by Jansen et al. [21], the mean echo intensity of the rectus femoris muscle in boys with DMD aged 4–6 years was found abnormal, but the mean echo intensity of the forearm flexors were normal up to 8–10 years of age. Our study showed the same tendency of gradual involvement of varied oral muscles, but with a later onset than in skeletal muscles with the first dystrophic change (i.e. the infiltration of fat and fibrous tissue) of the geniohyoid muscle in the AS (median age 8.3 years) and of the digastric muscles and superior longitudinal tongue muscle only in the LNAS. The echo intensity of the transverse tongue muscle was abnormal (z score >2) only in patients older than 25 years. This is in accordance with the findings in the murine model of DMD (mdx mice) in which the masseter, temporal and tongue muscles were also unequally affected, with the tongue the least implicated muscle [25]. Several studies concluded that craniofacial and oral muscles differ from skeletal muscles in their developmental pattern, functional properties and fiber-type composition [26]. Generally, ongoing muscle weakness gradually cause a secondary reduction of physical activity, leading at first to disuse, followed by strict muscle pathology in latter stages [27]. Although we observed dystrophic changes in the geniohyoid muscles in the AS, disuse cannot be an explanation for this finding, because the flexible oral muscles are submaximally activated during swallowing and speech [28]. We presume that the differences in incidence and degree of dystrophic changes between the skeletal and oral muscles may reflect the different properties and fiber composition

of these muscles and the ability to use oral muscles with limited force.

In our study, the thickness of the digastric muscles was within normal ranges. However, the thickness of the tongue was increased (>2 SD) in 70 % of the patients in the ENAS and LNAS. This muscle hypertrophy is also known from calf enlargement in DMD. Lower leg muscles were found to have a distinct clinical appearance as DMD progresses with selective muscle involvement, from which the underlying etiology is uncertain [29]. Calf-muscle hypertrophy with an increase in muscle fiber size (without infiltration of fatty tissue) was considered to be characteristic of the first stage of muscle change in DMD. It was called pseudohypertrophy if the echo intensity of the muscles exceeded normal values [30]. Marden et al. [31] hypothesized that this muscle hypertrophy occurred in spared muscles. Muscles of the tongue also retain their function longer and show the same tendency with selective muscle involvement. In the ENAS we found an increase in tongue thickness without increased echo intensity, which can be considered hypertrophy. We suggest that the macroglossia in the LNAS, based on the significant correlation between increased echo intensity and tongue thickness, is a pseudohypertrophic phenomenon.

Our results demonstrate that dysphagia in DMD patients is caused by dystrophic changes in submental muscles and the tongue, starting in the AS. Oral muscles become severely affected in the LNAS, resulting in reduced strength, which influences mostly the deglutition of solid food.

Rehabilitation in neuromuscular disorders can be focused on both recommendations for behavioral compensations and task-specific restorative training [32], taking into account the underlying pathophysiological processes. The primary aim in dysphagia rehabilitation is safety, i.e., preventing choking and aspiration pneumonia. In case of choking, the general advice is to take thickened liquids. However, this is not appropriate in this patient group. Our findings lead to the conclusion that in this patient group solid food causes the most oral phase problems and pharyngeal post-swallow residue. Based on the disturbed mechanisms it is suggested that these problems can be diminished by adjusting meals (more liquid and thick liquid than solid food) and drinking water during and after meals to clear the pharyngeal residue, because it is known from the literature that aspiration pneumonia can be caused by this post-swallow residue [24]. The value of these preliminary recommendations must be proved in future therapeutic trials as well as the value of task-specific restorative training in case of dysphagia in DMD.

Attention to possible dysphagia is necessary not only in LNAS of DMD [2], but also in the early stages of the disease. Further research is needed to study the influence of

medication, such as prednisone, on the involvement of oral muscles and on the clinical course of dysphagia in DMD.

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Conflicts of interest The authors declare that they have no conflict of interest.

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